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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	14

DATE MAILED: 11/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/914,364	Applicant(s) WACHER ET AL.	
	Examiner Brian S Kwon	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10-12,14-23,32-36,38-43,52-55 and 57-59* is/are pending in the application.

4a) Of the above claim(s) *1, 10-12, 14-22, 41, 42 and 57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23, 32-36, 38-40, 43, 52-55 and 58-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Summary of Action

I. As indicated in page 3, para. 3 of O.A. mailed February 12, 2003, no copies of publication have been supplied to the Office to find out the relevancy of the references submitted. Consequently, IDS filed February 25, 2002 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; or that portion which caused it to be listed; and all other information or that portion which caused it to be listed.

With respect to US patents (P1-P6) and Foreign patent documents (F1-F7), the examiner was able to obtain copies of references from the readily available USPTO internet data base and has initialed accordingly. However, cited Non-Patent Literature Documents (except D2, D31 and D41) have not been considered since those copies are not readily available to the examiner.

II. The rejection of claims 23, 32-36, 38-40, 43, 52-55 and 58-59 under 35 USC 112, first paragraph, will be maintained for the reason of record.

III. The rejection of claim 55 under 35 USC 112, second paragraph, will be maintained for the reason of record.

IV. The rejection of claims 23, 32, 34-36, 38-40, 43, 52 and 54-55 under 35 USC 102(b) as being anticipated by Salatinjants (US 4716173) will be maintained for the reason of record.

V. The rejection of claims 23, 32-36, 38-40, 43, 52-55 and 58-59 under 35 USC 102(b) as being anticipated by Shimamura et al. (US 5807564 A) will be maintained for the reason of record.

VI. The rejection of claims 23, 36, 38, 40, 43, 52-55 and 58 under 35 USC 102(b) as being anticipated by Xiong et al. (US 6299925 B1) will be maintained for the reason of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 23, 32-36, 38-40, 43, 52-55 and 58-59 are rejected under 35 USC 112, first paragraph.

This rejection is analogous to the original rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 55 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is analogous to the original rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

3. Claims 23, 32, 34-36, 38-40, 43, 52 and 54-55 are rejected under 35 U.S.C. 102(b) as being anticipated by Salatinjants (US 4716173).

This rejection is analogous to the original rejection.

4. Claims 23, 32-36, 38-40, 43, 52-55 and 58-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Shimamura et al. (US 5807564 A).

This rejection is analogous to the original rejection.

5. Claims 23, 36, 38, 40, 43, 52-55 and 58 are rejected under 35 U.S.C. 102(e) as being anticipated by Xiong et al. (US 6299925 B1).

This rejection is analogous to the original rejection.

Response to Arguments

6. Applicant's arguments filed August 12, 2003 have been fully considered but they are not persuasive.

In response to the examiner rejection of claim 55 under 35 USC 112, second paragraph, applicants state that claim 55 claims a reformulated oral composition that contains less than all the components of the existing pharmaceutical composition plus the gallic acid ester. In addition applicants state: "the claim cover pharmaceutical composition in which one or more of the components of the existing pharmaceutical composition is absent. Such a claim encompasses a clearly defined set of possible combinations and is not indefinite".

The examiner determines that claim 55 is vague and unclear and leaves the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of

the subject-matter of said claims unclear. Applicants still fail to clarify specifically which components should be present in the reformulated oral composition.

With respect to applicants comment that "reformulating an existing oral pharmaceutical composition" is not present in Claims 23, 32-36, 38-40 and 58, the examiner likes to thank applicants to point out the error in page 4, No. 6 in the O.A. mailed on February 12, 2003. It appears that the examiner inadvertently omitted term "formulating an oral pharmaceutical composition" or. Regardless of the examiner's omission of "formulating an oral pharmaceutical composition", the examiner believes that whole context of the 35 USC 112, first paragraph, rejection would have been apparent to readers why the scope of claims 23, 32-36, 38-40, 43, 52-55 and 8-59 are not enabled by the specification. Therefore, the examiner maintains the original rejection.

Applicants' argument takes position that the Patent Office has failed to provide any reason for objectively doubting the validity of any statements relied on for enabling support. The examiner disagrees with this argument.

The specification states (page 7, line 20 thru page 8, line 5): "the word "drug" is a chemical capable of administration to an organism which modifies or alters the organism's physiology. More preferably, the word "drug" as used herein is defined as any substance intended for use in the treatment or prevention of disease...The term drug also includes compounds that have the indicated properties that are not yet discovered or available in the U.S...". In other words, the scope of instantly claimed "an oral pharmaceutical composition", "a

pharmaceutical compound" or "an existing oral pharmaceutical composition" or "an active compound of an existing oral pharmaceutical composition" is purported to cover all compounds or compositions or substances or drugs, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Furthermore, with respect to the claim 40 limitation, the claimed pharmaceutical compound covers plethora of possible compounds that may or may not be addressed by the instantly claimed compounds or compositions.

As stated in previous O.A. (page 5, lines 3-10), the specification discloses that gallic acid esters (e.g., epicatechin gallate, epigallocatechin gallate, gallocatechin gallate and tannic acid) are useful in a method to increase the bioavailability of orally administered pharmaceutical compounds or compositions that are well known in the art as being poor-bioavailability-drugs (e.g., nifedipine, amiodarone, ketoconazole, cyclosporine, diltiazem, drythromycin, verapamil). The present invention is based on the activity of the claimed gallic acid esters (e.g., epicatechin gallate, epigallocatechin gallate, gallocatechin gallate and tannic acid) in inhibiting drug cytochromes P450 biotransformation, more specifically CYP3A, in the gut to increase drug bioavailability. In other words, the specification provides sufficient enabling disclosure for (i) formulating the specific oral pharmaceutical composition or drugs or (ii) reformulating the specific known oral pharmaceutical composition or drugs that undergoes cytochrome P450 CYP3A metabolism. However, the instant specification fails to provide sufficient information regarding (a) how to make all possible compositions or drugs that may or may not be addressed by the claimed invention; and (b) how to ascertain which drugs would work similarly to the examples disclosed in the specification (e.g., nifedipine, amiodarone, ketoconazole, cyclosporine, diltiazem, drythromycin, verapamil) without undue amount of experimentation.

As stated above, all of disclosed examples in the specification are drawn to drugs that undergo P450 CYP3A metabolism and the efficacy of the gallic acid ester in inhibiting P450 CYP3A metabolism, thereby improving the bioavailability of the drugs. The specification does not recite drugs that may not be metabolized by P450 CYP3A. Furthermore, the specification does not provide adequate direction or guidance whether the gallic acid ester having CYP3A inhibiting activity is going to improve the bioavailability of the drugs that may not be metabolized by P450 CYP3A. In view of the amount of guidance present in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Applicants state in page 5, para. 6 of the response filed August 12, 2003: "claims 58 and 59 fail to recite tannic acid. Hence, since Salatinjants fails to teach each and every limitation of the above Claims, the cited reference fails to anticipated the invention recited in these Claims". It is not clear why applicants request for withdrawal of claims 58 and 59 under 35 USC 102(b) over Salatinjants which was not included in the rejection. Reviewing of the Office Action mailed February 12, 2003, the examiner cannot find the alleged inclusion of claims 58 and 59 in 35 USC 102(b) rejection over Salatinjants. Only claims 23, 32, 34-36, 38-40, 43, 52 and 54-55 were rejected under 35 USC 102(b) as being anticipated by Salatinjants (page 2 under the heading of Summary of Action and page 7 under the heading of 35 USC 102(b) rejection).

Applicants' argument takes position that anticipation of a claim requires that the reference teach every element of the claim. Applicants allege that the present invention refers to

increasing the systemic drug concentration over time where systemic drug concentration refers to the concentration of drug present in the bodily fluids, such as serum, plasma or blood and the tissues bathed by the systemic fluids, including the skin. Furthermore, applicants allege that Salatinjants fails to teach the claimed "increasing the fraction of the oral dose that reaches bodily fluids".

This is spurious argument. Unlike applicants' argument, prolonging the residence time of a drug in the circulating plasma leads to a higher bioavailability of the drug at its target (see also Emerson et al., "Antitumor Efficacy, Pharmacokinetics, and Biodistribution of NX 211: A low-Clearance Liposomal Formulation of Lurtotecan", Clinical Cancer Research, Vol. 6, 2903-2912, July 2000; Mehta et al., "In Vivo Release Performance of Nifedipine in Dogs from a Novel EUDRAGIT-Based Multi-Unit Erosion Matrix", Drug Delivery, Volume 2, No. 1, 2002). In alternative, regardless of different underlying mechanism involved as applicants alleged, the prior art method of preparing quinine or sulfa drugs (e.g., sulfamethizone, sulfamethoxazole and sulfasalazine) or cinchona alkaloids by admixing the drugs with tannic acid would inherently possess such property or characteristic as the claimed method. Therefore, the reference anticipates the claimed invention.

Applicants' argument takes position that Shimamura fails to teach that tea catechins and tea extracts increase the bioavailability of antibiotics when formulated as an oral pharmaceutical composition, therefore, Shimumura fails to anticipate the present invention.

Applicants are correct that Shimamura fails to teach whether tea catechins and tea extracts increase the bioavailability of antibiotics. However, such characteristics or properties

must be inherently presented in referenced improved antiobiotic composition. The referenced method inherently possessing a therapeutic effect for the same ultimate purpose as disclosed as the applicants anticipates the applicants' claims even absent explicit recitations of the mechanism of action.

Applicants' argument takes position that Xiong fails to teach every element of the invention claimed in the present application and thus is not an anticipatory reference. Applicants allege that Xiong teaches a formulation which increases the bioavailability of green tea polyphenols not a method of using gallic acid esters to increase the bioavailability of other pharmaceutical compounds in a pharmaceutical composition, as claimed in the present invention.

Applicants are correct that Xiong fails to teach whether the green tea extract increases the bioavailabilty of other pharmaceutical compounds. However, such characteristics or properties must be inherently presented in referenced effervescent green tea extract formulation prepared by admixing a concentrated green tea plant extract having (-)epigallocatechin gallate with vitamins, ionic minerals and Herb/botanical extract. As indicated above, the referenced method inherently possessing a therapeutic effect for the same ultimate purpose as disclosed as the applicants anticipates the applicants' claims even absent explicit recitations of the mechanism of action.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703)308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600